

10/528179

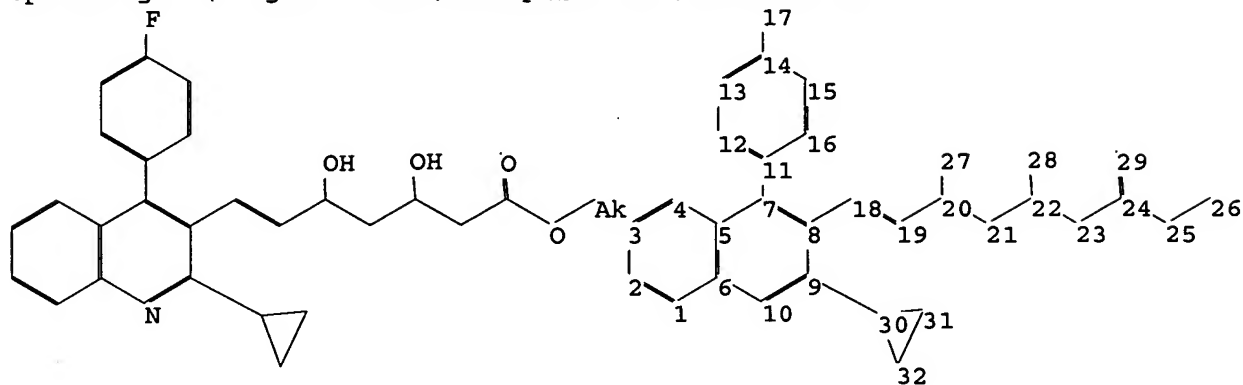
***** STN Columbus *****

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chain nodes :

17 18 19 20 21 22 23 24 25 26 27 28 29

ring nodes :

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 30 31 32

chain bonds :

7-11 8-18 9-30 14-17 18-19 19-20 20-21 20-27 21-22 22-23 22-28 23-24
24-25 24-29 25-26

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 8-9 9-10 11-12 11-16 12-13 13-14
14-15 15-16 30-31 30-32 31-32

exact/norm bonds :

20-27 22-28 24-25 24-29 25-26 30-31 30-32 31-32

exact bonds :

7-11 8-18 9-30 14-17 18-19 19-20 20-21 21-22 22-23 23-24

normalized bonds :

1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 8-9 9-10 11-12 11-16 12-13 13-14
14-15 15-16

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:CLASS 18:CLASS 19:CLASS
20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS
28:CLASS 29:CLASS 30:Atom 31:Atom 32:Atom

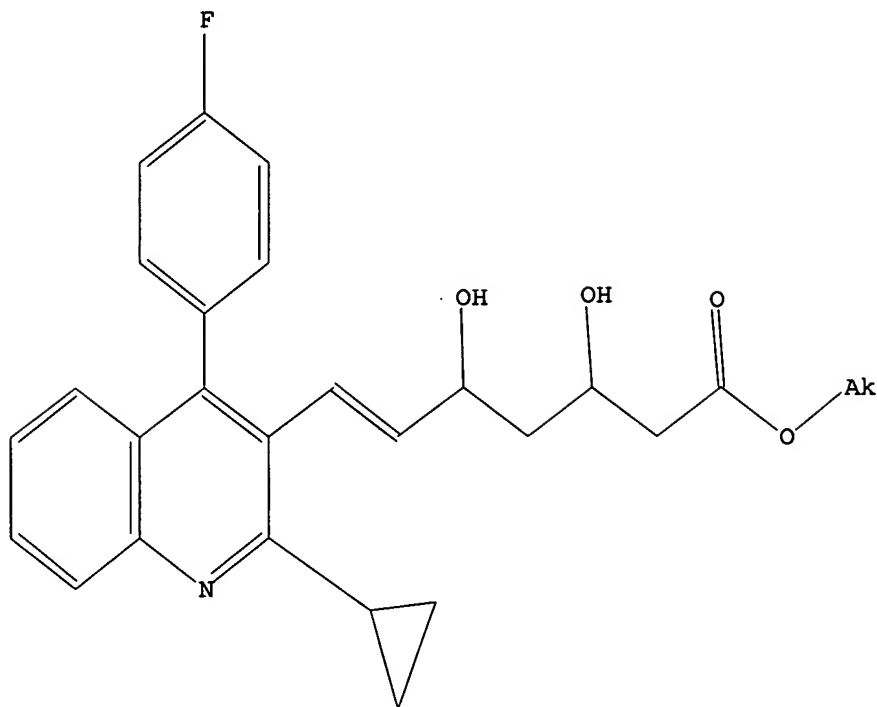
10/528179

L1 STRUCTURE UPLOADED

=> d l1

L1 HAS NO ANSWERS

L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1 full

L3 24 SEA SSS FUL L1

=> file ca

=> s l3

L4 32 L3

=> s liquid chromatograph?

651439 LIQUID

394430 CHROMATOGRAPH?

L5 83200 LIQUID CHROMATOGRAPH?

(LIQUID (W) CHROMATOGRAPH?)

=> s l4 and l5

L6 4 L4 AND L5

=> s l4 and resolv?

178031 RESOLV?

L7 3 L4 AND RESOLV?

=> s l6 or l7

L8 6 L6 OR L7

10/528179

=> d ibib abs fhitr 1-6

L8 ANSWER 1 OF 6 CA COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

TITLE: Method for producing ethyl

(3R,5S,6E)-7-[2-cyclopropyl-

4-(4-fluorophenyl)quinolin-3-yl]-3,5-dihydroxy-6-

heptenoate

INVENTOR(S): Onishi, Atsushi; Tachibana, Koza

PATENT ASSIGNER(S): Daicel Chemical Industries, Ltd., Japan; Nissan

Chemical Industries, Ltd.

SOURCE: PCT Int. Appl., 28 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-----------------|------------|
| WO 2004094389 | A1 | 20041114 | WO 2004-JP5894 | 20040423 |
| W: | AB, AG, AL, AM, AN, AR, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, GU, HK, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RM: | BW, GH, GM, KE, LS, MM, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CP, CO, CI, CM, CA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| EP 1623978 | A1 | 20060208 | EP 2004-729193 | 20040423 |
| R: | CH, DE, FR, GB, IT, LI, IE | | | |
| PRIORITY APPLN. INFO.: | | | JP 2003-119807 | A 20030424 |
| | | | WO 2004-JP5894 | M 20040423 |

AB Disclosed is a method for producing Et (3R,5S,6E)-7-[2-cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl]-3,5-dihydroxy-6-heptenoate (I) from a solution containing a mixture of optical isomers of Et (6E)-7-[2-cyclopropyl-4-(4-fluorophenyl)quinoline-3-yl]-3,5-dihydroxy-6-heptenoate by means of the liquid chromatog. using a packing material having a carrier and, carried thereon, a polysaccharide derivative, characterized in that a part or all of the hydrogen atoms of the hydroxyl groups and amino groups of the polysaccharide derivative are substituted with one or more substituents, such as a carbamoyl group wherein one hydrogen atom is substituted with an aromatic group having a specific alkyl group. The method allows the production of the above (3R,5S,6E)-isomer I with enhanced productivity compared to a conventional method. Thus, 100 g cellulose and 794 g 4-isopropylphenyl isocyanate were stirred in pyridine at reflux for 60 h to give 84.6% cellulose tris(4-isopropylcarbamate) (II) which (100 g) was dissolved in 600 mL acetone and added to 3-aminopropylated silica gel (400 g), followed

L8 ANSWER 1 OF 6 CA COPYRIGHT 2006 ACS on STN (Continued)

by evapn. of the solvent under reduced pressure to give II-supported on silica gel as a packing material. This packing material was packed in a stainless steel column (0.46 cm diam. X 25 cm length) by the slurry method

to give a HPLC column. A mixt. of Et (3R,5S,6E)- and (3S,5R,6E)-7-[2-cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl]-3,5-dihydroxy-6-heptenoate was sepd. by the HPLC column prepd. above using n-hexane/2-propanol (50/50

vol./vol. ratio) as the eluent at 40°.

IT 147008-20-6, Ethyl rel-(3R,5S,6E)-7-[2-Cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl]-3,5-dihydroxy-6-heptenoate

RL: PEP (Physical, engineering or chemical process); PYP (Physical process); PROC (Process)

(method for producing Et (3R,5S,6E)-7-[2-cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl]-3,5-dihydroxy-6-heptenoate by liquid chromatog. separation using polysaccharide carbamate derivative supported on

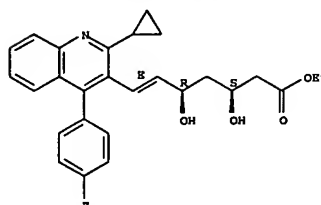
silica gel)

RN 147008-20-6 CA

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L8 ANSWER 2 OF 6 CA COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 140:287282 CA

TITLE: Purification of a 3,5-dihydroxy-6-heptenoate isomer

Yoshimura, Yuji; Yasukawa, Masami; Morikio, Syuji;

Matsumoto, Hiroo; Takada, Yasutaka; Adachi, Michiaki

Nissan Chemical Industries, Ltd., Japan

SOURCE: PCT Int. Appl., 29 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-----------------|------------|
| WO 2004026838 | A1 | 20040401 | WO 2003-JP11643 | 20030911 |
| W: | AB, AG, AL, AM, AN, AR, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, GU, HK, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RM: | BW, GH, GM, KE, LS, MM, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CP, CO, CI, CM, CA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| CA 2499335 | AA | 20040401 | CA 2003-249935 | 20030911 |
| AU 2003260963 | A1 | 20040408 | AU 2003-260963 | 20030911 |
| EP 1539698 | A1 | 20050615 | EP 2003-797579 | 20030911 |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | |
| JP 2006500405 | T2 | 20060105 | JP 2004-537553 | 20030911 |
| PRIORITY APPLN. INFO.: | | | JP 2002-275015 | A 20020920 |
| | | | WO 2003-JP11643 | M 20030911 |

OTHER SOURCE(S): MARPAT 140:287282

GI

L8 ANSWER 2 OF 6 CA COPYRIGHT 2006 ACS on STN (Continued)

liq. chromatog. on silica gel.

IT 167073-19-0P

RL: PUR (Purification or recovery); PREP (Preparation)

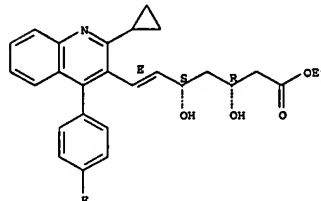
(purification of a 3,5-dihydroxy-6-heptenoate isomer)

RN 167073-19-0 CA

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)

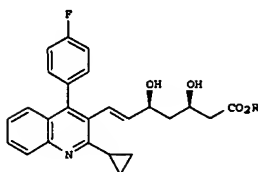
Absolute stereochemistry.

Double bond geometry as shown.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT



AB An alkyl (3R,5S)-7-[2-cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl]-3,5-dihydroxy-6-heptenoate I (R = alkyl), which is an intermediate for a cholesterol-reducing agent (a HMG-CoA reductase inhibitor), is purified

L8 ANSWER 3 OF 6 CA COPYRIGHT 2006 ACS on STN
 137:384764 CA
 TITLE: Process for preparation of optically active

7-[2-(cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl)-3,5-dihydroxyhept-6-enoic acid ethyl ester
 INVENTOR(S): Nishino, Shigeyoshi; Matsushita, Akio; Yokoyama, Shuji; Kawachi, Yasuhiro; Sasaki, Hiroshi
 PATENT ASSIGNER(S): UBE Industries, Ltd., Japan
 SOURCE: PCT Int. Appl., 26 pp.
 CODES: PIXXD2

DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-----------------|------------|
| WO 2003027073 | A1 | 20030403 | WO 2002-JP9638 | 20020919 |
| W: | AB, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RM: | GH, GM, KE, LS, MM, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CP, CO, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TO | | | |
| JP 2005255522 | A2 | 20050922 | JP 2001-284633 | 20010919 |
| JP 2005255523 | A2 | 20050922 | JP 2001-284634 | 20010919 |
| PRIORITY APPLN. INFO.: | | | JP 2001-284633 | A 20010919 |
| | | | JP 2001-284634 | A 20010919 |

AB This invention pertains to prep method of (3R,5S)-7-[2-(cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl)-3,5-dihydroxyhept-6-enoic acid Et ester useful as an intermediate for an HMG-CoA reductase inhibitor (cholesterol-lowering agent) in high yield by reacting an amine salt of (3R,5S)-7-[2-(cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl)-3,5-dihydroxyhept-6-enoic acid with an alc. in a solvent in the presence of an acid, or by a method comprising reacting the salt with an esterifying agent in a solvent in the presence of a base. For example, 7-[2-(cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl)-3,5-dihydroxyhept-6-enoic acid was reacted with PhCH₂NH₂ in AcOEt to obtain 7-[2-(cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl)-3,5-dihydroxyhept-6-enoic acid benzylamine salt (94.9%). The above salt was resolved with THF to give (3R,5S)-7-[2-(cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl)-3,5-dihydroxyhept-6-enoic acid benzylamine salt (60.0%, 99.1% ee, 99.8% de). The above optically active salt was reacted with EtOH in the presence of concentrated aqueous HCl to afford (3R,5S)-7-[2-(cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl)-3,5-dihydroxyhept-6-enoic acid Et ester

L8 ANSWER 4 OF 6 CA COPYRIGHT 2006 ACS on STN
 137:384764 CA
 TITLE: Process for producing (3R,5S)-7-substituted-3,5-dihydroxyhept-6-enoic acid
 INVENTOR(S): Nishino, Shigeyoshi; Yokoyama, Shuji; Kawachi, Yasuhiro; Sasaki, Hiroshi
 PATENT ASSIGNER(S): UBE Industries, Ltd., Japan
 SOURCE: PCT Int. Appl., 33 pp.
 CODES: PIXXD2

DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-----------------|------------|
| WO 20020292570 | A1 | 20021122 | WO 2002-JP4710 | 20020515 |
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| RM: | GH, GM, KE, LS, MM, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CP, CO, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TO | | | |
| JP 2005047803 | A2 | 20050224 | JP 2001-145358 | 20010515 |
| PRIORITY APPLN. INFO.: | | | JP 2001-145358 | A 20010515 |

OTHER SOURCE(S): MARPAT 137:384764
 GI

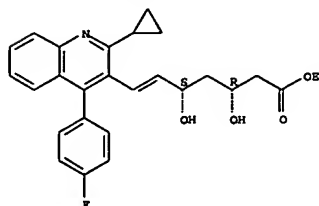
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Disclosed is a process for producing a (3R,5S)-7-[2-(cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl)-3,5-dihydroxyhept-6-enoic acid represented by the formula (I) which comprises optically resolving with an achiral amine compound a mixture of optical isomers of a 7-[2-(cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl)-3,5-dihydroxyhept-6-enoic acid represented by the formula (II). The optical resolution involves contacting II with an achiral amine to form II achiral amine salt, recrystg. the salt to form I achiral amine salt, and contacting the I achiral recrystn. amine salt with an acid to give I. This process does not use expensive chiral amines and is suitable for industrial preparation of I which is an intermediate for an anticholesteremic agent (HMG-CoA reductase inhibitor). Thus, 4.21 g II (preparation given), 1.07 g benzylamine, and 30 mL EtOAc were added to a 50 mL flask and cooled to 0° with stirring, upon which crystals precipitated. The precipitated crystals were filtered, washed with EtOAc cooled at 0°, and dried under reduced pressure to give 94.9% II benzylamine salt. II benzylamine salt (4.22 g) and 84 mL THF were added to a 100 mL flask, warmed to 50° with stirring to give a homogeneous solution, and cooled to 0°, upon which crystals precipitated. The precipitated crystals were

L8 ANSWER 3 OF 6 CA COPYRIGHT 2006 ACS on STN (Continued)
 (100%), which was crystd. from (i-Pr)₂O and heptane to produce cryst. sample (91.0%, 99.9% ee, 99.8% de).

IT RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
 (process for preparation of optically active 7-[2-(cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl)-3,5-dihydroxyhept-6-enoic acid Et ester)
 RN 172336-32-2 CA
 CN 6-Heptenoic acid, 7-[2-(cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
 Double bond geometry unknown.

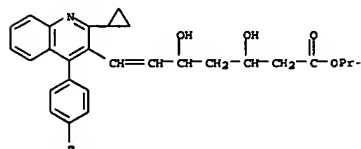


REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L8 ANSWER 4 OF 6 CA COPYRIGHT 2006 ACS on STN (Continued)
 and washed with 42 mL THF cooled at 0°. This procedure was repeated twice to give 2.52 g I benzyl amine salt (60.0%) which (2.11 g) and 10 mL MeOH were added to a 50 mL flask, adjusted to pH 3.5 by adding

1 M aq. HCl, and extd. with 10 mL EtOAc twice, followed by drying the EtOAc ext. over anhyd. MgSO₄ and concn. to give 1.66 g I (99.0%).
 IT 475645-78-4P, 7-[2-(cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl)-3,5-dihydroxyhept-6-enoic acid isopropyl ester
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of (3R,5S)-7-[2-(cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl)-3,5-dihydroxyhept-6-enoic acid by optical resolution using achiral amine via formation of achiral amine salt, recrystn., and treatment with acid)
 RN 475645-78-4 CA
 CN 6-Heptenoic acid, 7-[2-(cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, 1-methylethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L8 ANSWER 5 OF 6 CA COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 136:325435 CA
 TITLE: Process for producing optically active ethyl

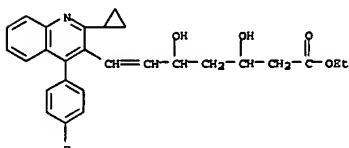
(3R,5S,6R)-7-[2-(cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl)]-3,5-dihydroxy-6-heptenoate
 INVENTOR(S): Onishi, Atsushi; Murazumi, Koichi; Tachibana, Kozo
 PATENT ASSIGNEE(S): Daicel Chemical Industries, Ltd., Japan; Nissan Chemical Industries, Ltd.
 SOURCE: PCT Int. Appl., 30 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-----------------------|--|----------|-----------------|------------|
| WO 2002030903 | A1 | 20020418 | WO 2001-JP9000 | 20011012 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW | | | |
| RM: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CP, CO, CI, CM, CA, CN, GQ, GW, ML, MR, NE, SN, TD, TU | | | |
| AU 2001095926 | A5 | 20020422 | AU 2001-95926 | 20011012 |
| EP 1334967 | A1 | 20030813 | EP 2001-976679 | 20011012 |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | |
| US 2005075502 | A1 | 20050407 | US 2002-398915 | 20030709 |
| US 6946557 | B2 | 20050920 | | |
| PRIORITY APPL. INFO.: | | | JP 2000-314245 | A 20001013 |
| | | | WO 2001-JP9000 | W 20011012 |

AB The process for producing an optically active isomer of Et 7-[2-(cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl)]-3,5-dihydroxy-6-heptenoate comprises optically resolving, at a high efficiency, a mixture of optical isomers of the compound, characterized in that a packing comprising a support and cellulose tris(4-chlorophenylcarbamate) deposited thereon in a specific proportion is used to chromatog. isolate the target isomer under such conditions as to result in a specific retention volume. The title compound is an intermediate for the known hypolipemic NK 104.
 IT 121661-13-0
 RL: ANT (Analyte); ANST (Analytical study)
 (process for producing optically active Et 7-[2-(cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl)]-3,5-dihydroxy-6-heptenoate)
 RN 121661-13-0 CA
 CN 6-Heptenoic acid, 7-[2-(cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl)]-3,5-dihydroxy-, ethyl ester (9CI) (CA INDEX NAME)

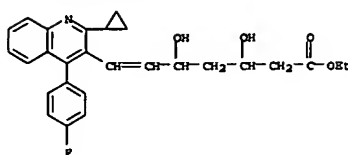
L8 ANSWER 6 OF 6 CA COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 130:316585 CA
 TITLE: Chiral separation of a pharmaceutical intermediate by a simulated moving bed process
 AUTHOR(S): Nagamatsu, S.; Murazumi, K.; Makino, S.
 CORPORATE SOURCE: Daicel Chemical Ind., Chiyoda-ku, Tokyo, 100, Japan
 SOURCE: Journal of Chromatography, A (1999), 832(1 + 2), 55-65
 CODEN: JCRABY; ISSN: 0021-9673

PUBLISHER: Elsevier Science B.V.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The chiral separation of a pharmaceutical intermediate by a simulated moving bed (SMB) system on a pilot-scale is described. The operating conditions were chosen from results simulated by the software, help, developed by Novasep, based upon data from a single column. The productivity of the SMB system is tested by the separation of an ester of quinoline mevalonic acid at various internal flow-rates. The eluent consumption is also discussed. The step time to switch the ports to enter or withdraw solns. is one of important factors influencing the productivity.
 IT 121661-13-0P, DOLE
 RL: ANT (Analyte); PUR (Purification or recovery); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation);
 USES (Uses)
 (chiral separation of pharmaceutical intermediate by simulated moving bed process)
 RN 121661-13-0 CA
 CN 6-Heptenoic acid, 7-[2-(cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl)]-3,5-dihydroxy-, ethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
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L8 ANSWER 5 OF 6 CA COPYRIGHT 2006 ACS on STN (Continued)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
 FORMAT

10/528179

=> s l4 not l8

L9 26 L4 NOT L8

=> d ibib abs fhitstr 1-26

L9 ANSWER 1 OF 26 CA COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 143:139169 CA
 TITLE: Preparation of crystal form of pitavastatin calcium
 INVENTOR(S): Ohara, Yoshio; Takada, Yasutaka; Matsumoto, Hiroo; Yoshida, Akihiro
 PATENT ASSIGNER(S): Nissan Chemical Industries, Ltd., Japan
 SOURCE: PCT Int. Appl., 21 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|---------------------------|-----------------|----------|
| WO 2005063711 | A1 | 20050714 | WO 2004-JP19451 | 20041217 |
| W: AR, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, GU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TO | | | | |
| PRIORITY APPL. INFO.: | | JP 2003-431788 A 20031226 | | |

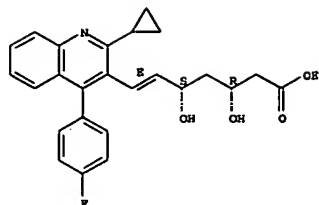
AB A method for producing a drug substance of crystalline pitavastatin calcium excellent in stability, is presented. In the production of a compound (pitavastatin calcium) the water content is adjusted to a level of 5-15%, and the crystal form is controlled to be crystal form A, thereby to obtain the drug excellent in stability.

IT 167073-19-0
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of crystal form of pitavastatin calcium)

RN 167073-19-0 CA
 CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3R,5S,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.

L9 ANSWER 1 OF 26 CA COPYRIGHT 2006 ACS on STN (Continued)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

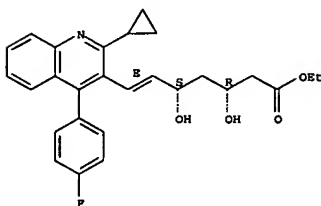
L9 ANSWER 2 OF 26 CA COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 142:481922 CA
 TITLE: Asymmetric reduction using biocatalytic reactions
 AUTHOR(S): Okano, Kazuya; Ueda, Makoto
 CORPORATE SOURCE: API Business Division, API Corporation, Japan
 SOURCE: Speciality Chemicals Magazine (2004), 34(11), 40-41
 CODEN: SPCHEM; ISSN: 0262-2062
 PUBLISHER: DMG World Media (uk) Ltd.
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB An enzyme expressed in a recombinant microorganism exhibited activity for the preparation of Pitavastatin Et ester by diastereoselective reduction of the 3-keto-5-hydroxy and double enantioselective reduction of the 3,5-diketo precursors.

IT 167073-19-0P, Pitavastatin ethyl ester
 RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
 (asym. reduction using biocatalytic reactions)

RN 167073-19-0 CA
 CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3R,5S,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



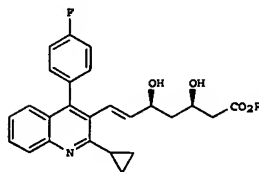
REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L9 ANSWER 3 OF 26 CA COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 142:392105 CA
 TITLE: A process for producing high-purity 3,5-dihydroxy-6-heptenoic acid derivatives, useful as medicinal intermediates
 INVENTOR(S): Yoshimura, Yuji; Yasukawa, Masami; Morikiyo, Syuji; Takada, Yasutaka; Matsumoto, Hiroo
 PATENT ASSIGNER(S): Nissan Chemical Industries, Ltd., Japan
 SOURCE: PCT Int. Appl., 24 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

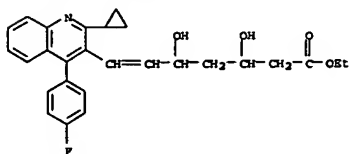
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|---------------------------|-----------------|----------|
| WO 2005033083 | A1 | 20050414 | WO 2004-JP14289 | 20040922 |
| W: AR, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, GU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TO | | | | |
| PRIORITY APPL. INFO.: | | JP 2003-346019 A 20031003 | | |

OTHER SOURCE(S): MARPAT 142:392105
 GI



AB The invention relates to a process for producing a high-purity 3,5-dihydroxy-6-heptenoic acid derivs. of formula I (R is alkyl). An alc.-containing solvent was employed in a process for obtaining an active isomer by optical resolution
 IT 121661-13-0P, DOLE
 RL: PUR (Purification or recovery); PREP (Preparation)
 (process for producing high-purity 3,5-dihydroxy-6-heptenoic acid

L9 ANSWER 3 OF 26 CA COPYRIGHT 2006 ACS on STN (Continued)
 derivs. useful as medicinal intermediates)
 RN 121661-13-0 CA
 CN 6-Hydroxyenoic acid, 7-(2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl)-3,5-
 dihydroxy-, ethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

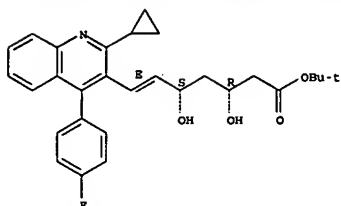
| | | | |
|-------------------------|---|----|---------------------------|
| L9 | ANSWER 4 OF 26 | CA | COPYRIGHT 2006 ACS on STN |
| ACCESSION NUMBER: | 141:230683 | CA | |
| TITLE: | Crystalline forms of pitevastatin calcium | | |
| INVENTOR(S): | Van Der Scheet, Paul Adriaens; Blatter, Fritz; Seeliger, Martin; Schoening, Kai-Uwe | | |
| PATENT ASSIGNER(S): | Ciba Specialty Chemicals Holding Inc., Switz. | | |
| SOURCE: | PCT Int. Appl., 33 pp. | | |
| | CODEN: PIXXD2 | | |
| DOCUMENT TYPE: | Patent | | |
| LANGUAGE: | English | | |
| FAMILY ACC. NUM. COUNT: | 1 | | |
| PATENT INFORMATION: | | | |

[illegible]

AB The present invention is directed to new crystalline forms of
Pitavastatin
hemicalcium salt, referred to hereinafter as polymorphic Forms A, B, C,
D,
E and F, as well as the amorphous form. Furthermore, the present
invention is directed to processes for the preparation of these
crystalline forms
and the amorphous form and pharmaceutical compns. comprising these
crystalline
forms or the amorphous form. The hemicalcium salt was prepared from
pitavastatin tert-Bu ester in tert-Bu ether and MeOH, NaOH added, and
aqueous
phase extracted with Me tert-Bu ether. Then CaCl2 was added to give a
form A.
IT 586966-54-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(crystalline forms of pitavastatin calcium)
RN 586966-54-3 CA
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-
dihydroxy-, 1,1-dimethylethyl ester, (3R,5S,6E)- (9CI) (CA INDEX NAME)

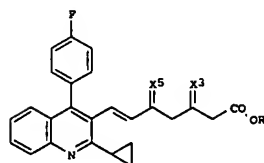
Absolute stereochemistry.
Double bond geometry as shown.

L9 ANSWER 4 OF 26 CA COPYRIGHT 2006 ACS on STN (Continued)



L9 ANSWER 5 OF 26 CA COPYRIGHT 2006 ACS ON STN
ACCESSION NUMBER: 140:41958 CA
TITLE: Process for the manufacture of organic compounds
INVENTOR(S): Storz, Thomas
PATENT ASSIGNER(S): Novartis AG, USA
SOURCE: U.S. Pat. Appl. Publ., 17 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

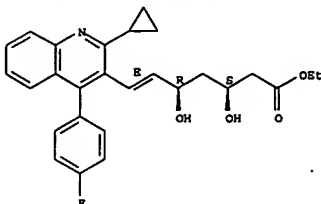
| | | | | |
|------------------------|--------|-----------|-----------------|------------|
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
| US 2003233001 | A1 | 20031218 | US 2003-428257 | 20030502 |
| US 6909003 | B2 | 20050621 | | |
| PRIORITY APPLN. INFO.: | | | GB 2002-10234 | A 20020503 |
| OTHER SOURCE(S): | MARPAT | 140:41958 | | |
| Q1 | | | | |



AB This invention relates to a process for the manufacture of analogs,
(3R,5R)-1-(CH₂)₂CH(OH)CH₂CH(OH)CH₂CO₂H and (3R,5S,6E)-
R₁CH=CHCH(OH)CH₂CH(OH)CH₂CO₂H [R₁ = cyclic statin analog residue], of
known HMG-CoA reductase inhibiting statins via an enantioselective
reduction using a ruthenium catalyst. Thus, p-toluenesulfonyl-hemicalcium salt
(3R,5S,6E)-1 (R = Et, X₃ = p-OH-o-H) was prepared
enantioselective reduction of 3,5-dioxo-ester (6E)-1 (R = Et, X₃ = X₅ =
O) catalyzed by
(1R,2R)-N-p-toluenesulfonyl-1,2-diphenylethylenediamine-Ru(II)-
p-cymene complex in DMF followed by treatment with Et₃N to give
3,5-diol-ester (3R,5S,6E)-1 (R = Et, X₃ = X₅ = p-OH-o-H) which
was subsequently converted to the target hemicalcium salt.
IT 167073-19-0P
RL: IMP (Industrial manufacture); RCT (Reactant); SPN (Synthetic
preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for asym. synthesis of analogs of statins via
enantioselective reduction using a ruthenium catalyst)
RN 167073-19-0 CA
CN 6-Heptenoic acid, 7-(2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl)-3,5-
dihydroxy-, ethyl ester, (3R,5S,6E)- (9CI) (CA INDEX NAME)

L9 ANSWER 7 OF 26 CA COPYRIGHT 2006 ACS on STN (Continued)
 the corresponding lactone [Ar = (un)substituted aryl, heteroaryl; R = H, alkyl, cycloalkyl, etc.] is disclosed. For example, ozonolysis of lactone II in methanol afforded aldehyde III in 83% yield. The process is claimed useful for the recycling of HMG-CoA reductase inhibitors unwanted, i.e. false (sic), diastereomers.
 IT 147008-20-6
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of aromatic aldehydes via the ozonolysis of aromatic alkenes)
 RN 147008-20-6 CA
 CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
 Double bond geometry as shown.

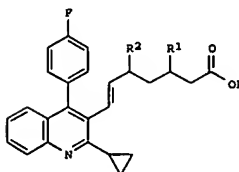


REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
 FORMAT

L9 ANSWER 8 OF 26 CA COPYRIGHT 2006 ACS on STN
 139:272910 CA
 ACCESSION NUMBER: 139:272910 CA
 TITLE: Ogataea minuta carbonyl reductase, encoding gene, and use for producing optically active alcohols
 INVENTOR(S): Hiraoka, Hirotooshi; Ueda, Makoto; Hara, Mari
 PATENT ASSIGNEE(S): Mitsubishi Chemical Corporation, Japan; Nissan Chemical Industries, Ltd.
 SOURCE: PCT Int. Appl., 54 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| WO 2003078634 | A1 | 20030925 | WO 2003-JP1262 | 20030318 |
| W: AB, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GR, GU, GM, HR, HU, ID, IL, IN, IS, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2479705 | AA | 20030925 | CA 2003-2479705 | 20030318 |
| AU 2003221082 | A1 | 20030929 | AU 2003-221082 | 20030318 |
| JP 2003339387 | A2 | 20031202 | JP 2003-74017 | 20030318 |
| EP 1491633 | A1 | 20041229 | EP 2003-712750 | 20030318 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| US 2005048633 | A1 | 20050303 | US 2004-943202 | 20040917 |
| PRIORITY APPLN. INFO.: | | | JP 2002-75921 | A 20020319 |
| | | | WO 2003-JP1262 | M 20030318 |

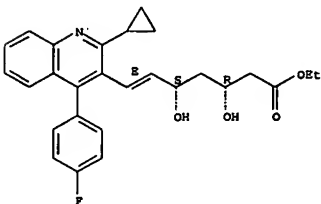
GI



I

L9 ANSWER 8 OF 26 CA COPYRIGHT 2006 ACS on STN (Continued)
 AB Provide a novel carbonyl reductase originating in a microorganism belonging to the genus Ogataea, an encoding gene, recombinant expression, and use for producing optically active alcs. By reducing ketones having general structures I (R = H, alkyl, aryl; R1 = :O, OH, (R)-OH; R2 = OH, (S)-OH, :O) with the use of carbonyl reductase, optically active alcs., in particular, (3R,5S)-(E)-7-[2-cyclopropyl-4-(4-fluorophenyl)-quinolin-3-yl]-3,5-dihydroxy-hept-6-enoic acid esters, can be produced. A novel carbonyl reductase was isolated from Ogataea minuta var. nonfermentans strain IPO 1473. Its substrate specificity was investigated with various ketones and aldehydes. Its activity for reduction of 2,2,2-Trifluoroacetophenone was significantly inhibited by Hg(II) ion and Zn(II) ion. Its gene was cloned, sequenced, and expressed in E. coli. The recombinant enzyme was used in production of (3R,5S)-(E)-7-[2-cyclopropyl-4-(4-fluorophenyl)-quinolin-3-yl]-3,5-dihydroxy-hept-6-enoic acid Et ester (3R,5S-DOLE) from (E)-7-[2-cyclopropyl-4-(4-fluorophenyl)-quinolin-3-yl]-3,5-dioxo-hept-6-enoic acid Et ester (DOXE) or 5S-(E)-7-[2-cyclopropyl-4-(4-fluorophenyl)-quinolin-3-yl]-5-hydroxy-3-oxohept-6-enoic acid Et ester (5S-MOLE), is described. The yield was 319 µg (31.9% with 100% e.e. optical purity), and 807 µg (80.7% with 97% e.e. optical purity), resp.
 IT 147073-19-0P, (3R,5S)-(E)-7-[2-cyclopropyl-4-(4-fluorophenyl)-quinolin-3-yl]-3,5-dihydroxy-hept-6-enoic acid ethyl ester
 RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
 (Ogataea minuta carbonyl reductase, encoding gene, and use for producing optically active alcs.)
 RN 147073-19-0 CA
 CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3R,5S,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



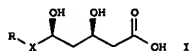
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
 FORMAT

L9 ANSWER 8 OF 26 CA COPYRIGHT 2006 ACS on STN (Continued)

L9 ANSWER 9 OF 26 CA COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 139:214343 CA
 TITLE: Process for the manufacture of HMG-CoA reductase inhibitory mevalonic acid derivatives
 INVENTOR(S): Sedelmaier, Gottfried; Mathes, Christian
 PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
 SOURCE: PCT Int. Appl., 44 pp.
 CODEN: PIXX22
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| WO 2003070717 | A1 | 20030828 | WO 2003-EP1738 | 20030220 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, MY, NZ, OM, PH, PL, PT, RO, RU, SC, SE, SG, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW | | | | |
| RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR | | | | |
| CA 2473075 | AA | 20030823 | CA 2003-2473075 | 20030220 |
| AU 2003218994 | A1 | 20030909 | AU 2003-218994 | 20030220 |
| EP 1478640 | A1 | 20041124 | EP 2003-714750 | 20030220 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, SE, HU, SK | | | | |
| BR 200307801 | A | 20041221 | BR 2003-7801 | 20030220 |
| JP 2005520818 | T2 | 20050714 | JP 2003-569624 | 20030220 |
| US 2005159480 | A1 | 20050721 | US 2003-504655 | 20030220 |
| ZA 2004005436 | A | 20050617 | ZA 2004-5436 | 20040708 |
| NO 2004003919 | A | 20040920 | NO 2004-3919 | 20040920 |
| | | | GB 2002-4129 | A 20020221 |
| | | | WO 2003-EP1738 | W 20030220 |

OTHER SOURCE(S): MARPAT 139:214343
 GI



AB Mevalonic acid derivs. I [R = cyclic residue; X = CH₂CH₂, CH:CH] are prepared by treating R1R2R3P:CHCOCH₂CO₂R4 [R1-R3 = (un)substituted Ph; R4 = aliphatic, cycloaliph., aromatic] with RCHO, reducing the resulting RCH:CHCOCH₂CO₂R4 in presence of a chiral metal BINAP or TsDPEN catalyst, treating the resulting alc. with an ester enolate, reducing the second oxo

L9 ANSWER 10 OF 26 CA COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 139:164712 CA
 TITLE: Asymmetric titanium mediated disilyloxydiene/aldehyde addition process for the preparation of 6-hydroxy-β-ketoesters.
 INVENTOR(S): Chen, Guang-Pei; Kapa, Prasad Koteswara; Loeser, Eric M.; Beutler, Ulrich; Zaugg, Werner; Girgis, Michael J.
 PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
 SOURCE: PCT Int. Appl., 53 pp.
 CODEN: PIXX22
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|-------------|
| WO 2003064382 | A2 | 20030807 | WO 2003-EP804 | 20030127 |
| WO 2003064382 | A3 | 20031221 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SE, SG, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW | | | | |
| RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR | | | | |
| US 2003208072 | A1 | 20031106 | US 2003-350615 | 20030124 |
| US 683588 | B2 | 20041228 | | |
| CA 2472340 | AA | 20030807 | CA 2003-2472340 | 20030127 |
| EP 1472227 | A2 | 20041103 | EP 2003-734696 | 20030127 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, SE, HU, SK | | | | |
| BR 2003007236 | A | 20041207 | BR 2003-7236 | 20030127 |
| JP 2005516064 | T2 | 20050602 | JP 2003-564005 | 20030127 |
| ZA 2004005219 | A | 20050617 | ZA 2004-5239 | 20040701 |
| US 2004249154 | A1 | 20041209 | US 2004-891357 | 20040714 |
| NO 2004003586 | A | 20041007 | NO 2004-3586 | 20040827 |
| | | | US 2002-352116P | P 20020128 |
| | | | US 2002-383188P | P 20020524 |
| | | | US 2003-350615 | A3 20030124 |
| | | | WO 2003-EP804 | W 20030127 |

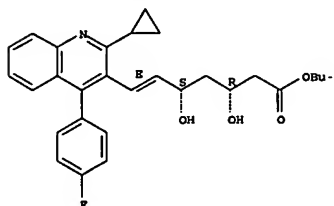
OTHER SOURCE(S): CASREACT 139:164712; MARPAT 139:164712
 GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB A process for the preparation of I [R1 = (un)substituted (cyclo)alkyl, aralkyl; R2-7 = H, halo, OH, (un)substituted (cyclo)alkyl, aralkyl, etc.] and analogs is disclosed. The process involves the Ti(OPr-i)4/(S)-BINOL

L9 ANSWER 9 OF 26 CA COPYRIGHT 2006 ACS on STN (Continued)
 s-group, and hydrolysing the ester group. Thus, ClCH₂COCH₂CO₂Et was treated with PPh₃ to give Ph₃P:CHCOCH₂CO₂Et which was treated with 2-cyclopropyl-4-(4-fluorophenyl)quinoline-3-carboxaldehyde to give (E)-5-[2-cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl]-3-oxopent-4-enoic acid Et ester. This ester was reduced with Ru[(1R,2R)-p-TsNCHPhCHPhNH](η-p-cymene) and treated with MeCOAc to give (E)-(S)-7-[2-cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl]-5-hydroxy-3-oxohept-4-enoic acid tert.-Bu ester which was reduced with MeOBSt₂ and hydrolyzed to give (E)-(3R,5S)-7-[2-cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl]-3,5-dihydroxyhept-4-enoic acid calcium salt.
 IT 586966-54-3P
 RL: IMP (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (process for the manufacture of HMG-CoA reductase inhibitory mevalonic acid derivative.)
 RN 586966-54-3 CA
 CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, 1,1-dimethylethyl ester, (3R,5S,6E)- (9CI) (CA INDEX NAME)

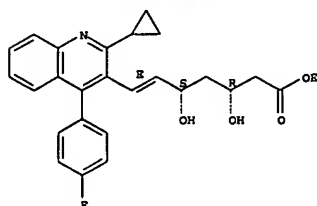
Absolute stereochemistry.
 Double bond geometry as shown.



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L9 ANSWER 10 OF 26 CA COPYRIGHT 2006 ACS on STN (Continued)
 mediated addn. of II [R1 = as above; R, R' = alkyl] to III [R2-7 = as above]. For instance, II [R1 = Et; R, R' = Me] (prepn. given) is reacted with III [R2 = F; R3-7 = H] (THF, 4Å mol. sieves, (S)-BINOL/Ti(OPr-i)4, 19°, 2 days) to give I [R1 = Et; R2 = F; R3-7 = H] in 81.6% yield (after purifn.) and the amt. of undesired enantiomer was below the limit of detection. Addnl. examples demonstrated sidechain manipulation (to the δ(S)-β(R)-ester) and subsequent conversion to pitavastatin (calcium salt) via the intermediacy of the 2H-pyranone. Exptl. details regarding mol. sieve prepn. and their use in a fixed bed reactor are given.
 IT 167073-19-0P
 RL: IMP (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (asym. titanium mediated disilyloxydiene/aldehyde addition process for preparation of 6-hydroxy-β-ketoesters)
 RN 167073-19-0 CA
 CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3R,5S,6E)- (9CI) (CA INDEX NAME)

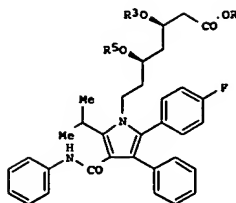
Absolute stereochemistry.
 Double bond geometry as shown.



L9 ANSWER 11 OF 26 CA COPYRIGHT 2006 ACS on STN
 138:204870 CA
 ACCESSION NUMBER:
 TITLE:
 INVENTOR(S):
 PATENT ASSIGNER(S):
 SOURCE:
 DOCUMENT TYPE:
 LANGUAGE:
 FAMILY ACC. NUM. COUNT:
 PATENT INFORMATION:

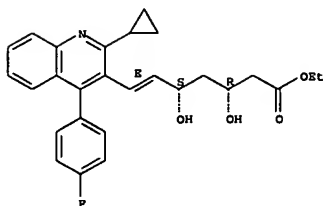
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-------------------|-------------|
| WO 2003016317 | A1 | 20030227 | WO 2002-US26012 | 20020816 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, GU, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NZ, NO, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RM: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2002099224 | A1 | 20020725 | US 2001-37412 | 20011024 |
| US 6528661 | B2 | 20030304 | | |
| CA 2450820 | AA | 20030227 | CA 2002-2450820 | 20020816 |
| US 2003114685 | A1 | 20030619 | US 2002-222556 | 20020816 |
| US 6777552 | B2 | 20040817 | | |
| EP 1425287 | A1 | 20040609 | EP 2002-759374 | 20020816 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | | |
| TR 200302281 | T2 | 20040921 | TR 2003-200302281 | 20020816 |
| CN 1543468 | A | 20041103 | CN 2002-815999 | 20020816 |
| JP 2005500382 | T2 | 20050106 | JP 2003-521239 | 20020816 |
| NZ 529913 | A | 20050324 | NZ 2002-529913 | 20020816 |
| ZA 2003009373 | A | 20041202 | ZA 2003-9173 | 20031202 |
| NO 2004001082 | A | 20040315 | NO 2004-1082 | 20040315 |
| US 2004176615 | A1 | 20040909 | US 2004-803414 | 20040318 |
| US 2005197501 | A1 | 20050908 | US 2005-120567 | 20050502 |
| PRIORITY APPLN. INFO.: | | | US 2001-312812P | P 20010816 |
| | | | US 2001-37412 | A 20011024 |
| | | | US 2000-249319P | P 20001116 |
| | | | US 2001-312144P | P 20010813 |
| | | | US 2001-326529P | P 20011001 |
| | | | US 2002-222556 | A3 20020816 |
| | | | WO 2002-US26012 | W 20020816 |

L9 ANSWER 11 OF 26 CA COPYRIGHT 2006 ACS on STN (Continued)
 US 2004-803414 A1 20040318
 OTHER SOURCE(S): MARPAT 138:204870
 GI



AB Processes for preparing hemicalcium salts of a statine
 $RCH(OH)CH_2CH(OH)CH_2CO_2H$ (R = statin organic radical selected from pravastatin, fluvastatin, cerivastatin, atorvastatin, rosuvastatin, pitavastatin, simvastatin, or lovastatin) from an ester derivative or protected ester derivative of the statin by using calcium hydroxide are provided. The ester or protected ester derivative is contacted with calcium hydroxide to obtain the calcium salt. Preferred statins are rosuvastatin, pitavastatin and atorvastatin, simvastatin and lovastatin. In processes beginning with a protected statin ester derivative, the protecting group is hydrolyzed during salt formation by contact with calcium hydroxide, or is contacted with an acid catalyst followed by contact with calcium hydroxide. Thus, diol-protected atorvastatin ester I (R = CMe₃, R₃R₅ = CMe₂) was treated with an 80% aqueous soln of AcOH at rt for 20 h to form the deprotected ester I (R = CMe₃, R₃ = R₅ = H) which was in turn dissolved in EtOH, treated with a saturated soln of Ca(OH)₂ containing Bu₄N⁺Br⁻ and stirred at 45° for 24 h to give atorvastatin hemicalcium salt I (R = 1/2Ca, R₃ = R₅ = H) in 77% yield for the two steps.
 IT 167073-19-0
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (processes for preparing calcium salt forms of statins)
 RN 167073-19-0 CA
 CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3R,5S,6E) - (9CI) (CA INDEX NAME)
 Absolute stereochemistry.
 Double bond geometry as shown.

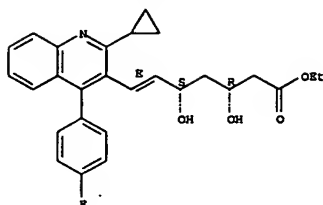
L9 ANSWER 11 OF 26 CA COPYRIGHT 2006 ACS on STN (Continued)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
 FORMAT

L9 ANSWER 12 OF 26 CA COPYRIGHT 2006 ACS on STN
 138:106481 CA
 ACCESSION NUMBER:
 TITLE:
 AUTHOR(S):
 Neohito;
 CORPORATE SOURCE:
 SOURCE:
 PUBLISHER:
 DOCUMENT TYPE:
 LANGUAGE:
 OTHER SOURCE(S):
 CASREACT 138:106481
 AB Highly enantioselective addition of diketene to aldehydes was achieved by using novel Schiff base-titanium alkoxide complexes. Up to 92% ee of 5-hydroxy-3-oxo esters was obtained. This procedure provides an efficient method for the asym. synthesis of potential inhibitors of HMG coenzyme reductase. Ligands included 2-(1,1-dimethylethyl)-6-[[[(1S)-1-(hydroxymethyl)-2-methylpropyl]imino]methyl]phenol (I), 2,4-bis[[1,1-dimethylethyl)-6-[[[(1S)-1-(hydroxymethyl)-2-methylpropyl]imino]methyl]phenol (II), 2,4-bis[[1,1-dimethylethyl)-6-[[[(1S)-1-(hydroxymethyl)-2-methylpropyl]imino]ethyl]phenol (III), etc. For example, the addition of benzaldehyde to diketene in the presence of I and titanium tetrakisopropoxide gave (8S)-8-hydroxy-β-oxobenzopentanoic acid 1-methylethyl ester in 62% yield and in 82% enantiomeric excess. Schiff base II was used as ligand in the reaction of diketene with (2E)-3-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-2-propenal to give (5S,6E)-7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-5-hydroxy-3-oxo-6-heptenoic acid Et ester. This product was an intermediate in the synthesis of (4R,6S)-(4R,6S)-6-[[[(1E)-2-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]ethenyl]tetrahydro-4-hydroxy-2H-pyran-2-one (niavastatin).
 IT 167073-19-0P, (3R,5S,6E)-7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-6-heptenoic acid ethyl ester
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (stereoselective addition of diketene to aldehydes promoted by chiral Schiff base-titanium alkoxide complexes)
 RN 167073-19-0 CA
 CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3R,5S,6E) - (9CI) (CA INDEX NAME)
 Absolute stereochemistry.
 Double bond geometry as shown.

L9 ANSWER 12 OF 26 CA COPYRIGHT 2006 ACS on STN (Continued)



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L9 ANSWER 13 OF 26 CA COPYRIGHT 2006 ACS on STN

138:24649 CA
 TITLE: Process for preparation of 2-cyclopropyl-4-(4-fluorophenyl)quinoline-3-carbaldehyde by oxonolysis of ethyl (6R)-3,5-dihydroxy-7-(2-cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl)hept-6-enoate
 INVENTOR(S): Matsumoto, Hiroo; Shimizu, Takanori
 PATENT ASSIGNER(S): Daicel Chemical Industries, Ltd., Japan; Nissan Chemical Industries, Ltd.
 SOURCE: PCT Int. Appl., 15 pp.
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-----------------------|--|----------|-----------------|------------|
| WO 2002098859 | A1 | 20021212 | WO 2002-JP4712 | 20020515 |
| W: | AB, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| CA 2448421 | AA | 20021212 | CA 2002-2448421 | 20020515 |
| EP 1391455 | A1 | 20040225 | EP 2002-776535 | 20020515 |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | |
| CN 1512984 | A | 20040714 | CN 2002-810769 | 20020515 |
| US 2004147750 | A1 | 20040729 | US 2003-479226 | 20031201 |
| PRIORITY APPL. INFO.: | | | JP 2001-162986 | A 20010530 |
| | | | JP 2001-208501 | A 20010709 |
| | | | WO 2002-JP4712 | W 20020515 |

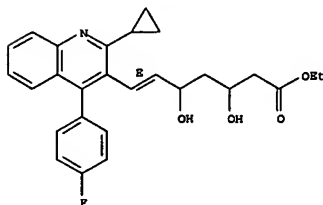
OTHER SOURCE(S): CASREACT 138:24649; MARPAT 138:24649
 GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Described is a process for preparing 2-cyclopropyl-4-(4-fluorophenyl)quinoline-3-carbaldehyde (I) which is important as an intermediate for the synthesis of drugs, i.e. HMG-CoA reductase inhibitor for cholesterol-lowering agent, efficiently from an unnecessary antipode, characterized by treating a compound represented by formula (II) or (III) (wherein A is -CHOH- or CO; and R is hydrogen, optionally branched C1-4

L9 ANSWER 13 OF 26 CA COPYRIGHT 2006 ACS on STN (Continued)
 alkyl, Ph, an alkali metal ion, or an alk. earth metal ion) with ozone and then conducting either redn. of the resulting compd. with an inorg. sulfur compd. or hydrogenolysis of the resulting compd. Thus, a soln. of 5.0 g Et (6E)-3,5-dihydroxy-7-(2-cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl)hept-6-enoate in 50 g MeOH was cooled to 0°, followed by introducing 1 g ozone(g) to the soln. at 0-5° over 1 h and removing excess ozone with N. To the resulting soln. was added dropwise a soln. of 0.85 g thiourea in 14.1 g H2O at 0-5° over 10 min, stirred at the same temp. for 1 h, treated with 26 g H2O, and stirred at 5° for 1 h to give, after filtering off pptd. crystals and washing them with 6 g aq. MeOH, and drying them, 2.81 g I (86.7% yield and 99.2% purity).
 IT 477950-34-8
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (process for preparation of 2-cyclopropyl-4-(4-fluorophenyl)quinoline-3-carbaldehyde as intermediate for HMG-CoA reductase inhibitor for cholesterol-lowering agent)
 RN 477950-34-8 CA
 CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (6E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L9 ANSWER 14 OF 26 CA COPYRIGHT 2006 ACS on STN

137:310823 CA
 TITLE: Method for preparing alkyl 7-quinolinyl-3,5-dihydroxyhept-6-enoate as intermediate for HMG-CoA reductase inhibitor
 INVENTOR(S): Tokunaga, Kenichi; Kozawa, Masami; Suzuki, Kenji
 PATENT ASSIGNER(S): Nissan Chemical Industries, Ltd., Japan
 SOURCE: PCT Int. Appl., 20 pp.
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-----------------------|--|----------|-----------------|------------|
| WO 2002081451 | A1 | 20021017 | WO 2002-JP2779 | 20020322 |
| W: | AB, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| CA 2442713 | AA | 20021017 | CA 2002-2442713 | 20020322 |
| EP 1375485 | A1 | 20040102 | EP 2002-707129 | 20020322 |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | |
| CN 1500079 | A | 20040526 | CN 2002-807845 | 20020322 |
| NZ 528149 | A | 20050527 | NZ 2002-528149 | 20020322 |
| RU 2260001 | C2 | 20050910 | RU 2003-132440 | 20020322 |
| ZA 2003007704 | A | 20041004 | ZA 2003-7704 | 20031002 |
| NO 2003004438 | A | 20031003 | NO 2003-4438 | 20031003 |
| US 2005014947 | A1 | 20050120 | US 2003-473132 | 20031006 |
| PRIORITY APPL. INFO.: | | | JP 2001-106820 | A 20010405 |
| | | | WO 2002-JP2779 | W 20020322 |

OTHER SOURCE(S): MARPAT 137:310823
 GI

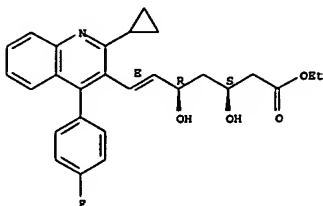
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB This document discloses a method for preparing alkyl 7-quinolinyl-3,5-dihydroxyhept-6-enoate represented by the formula I (R represents an alkyl group or an aryl group), characterized in that a compound represented by the formula II (R is as defined above), or a compound represented by the formula III (R is as defined above) is reduced by sodium borohydride in the presence of a boron compound represented by the formula R'OB(R'')2 (R' and R'' represent independently an alkyl group), and then the resulting reaction mixture is treated with an aqueous solution of hydrogen peroxide. (S)-I

10/528179

L9 ANSWER 14 OF 26 CA COPYRIGHT 2006 ACS on STN (Continued)
 (R = ethyl) was prepd. from (S)-11 (R = ethyl) by the title method.
 IT 147008-20-6DB, borane complex
 RL: BVP (Byproduct); CPS (Chemical process); PEP (Physical, engineering
 or chemical process); PREP (Preparation); PROC (Process)
 (preparation of alkyl 7-quinolinyl-3,5-dihydroxyhept-6-enoate by
 stereoselective reduction of alkyl 7-quinolinyl-5-hydroxy-3-oxohept-6-
 enoate by sodium borohydride in presence of boron compound)
 RN 147008-20-6 CA
 CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-
 dihydroxy-, ethyl ester, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
 Double bond geometry as shown.



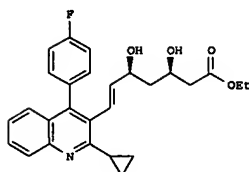
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR
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 RECORD. ALL CITATIONS AVAILABLE IN THE RE
 FORMAT

L9 ANSWER 15 OF 26 CA COPYRIGHT 2006 ACS on STN
 137:139496 CA
 ACCESSION NUMBER:
 TITLE: Process for producing (3R,5S)-(S)-7-[2-cyclopropyl-4-(4-fluorophenyl)-quinolin-3-yl]-3,5-dihydroxyhept-6-enoic acid ester and derivatives
 INVENTOR(S): Hara, Mari; Takuma, Yuki; Katsurada, Manabu; Akemi, Matsumoto, Youichi; Kasuga, Yuzo; Matanabe, Naoyuki
 PATENT ASSIGNEE(S): Mitsubishi Chemical Corporation, Japan; Nissan Chemical Industries, Ltd.
 SOURCE: PCT Int. Appl., 63 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| WO 2002063028 | A1 | 20010815 | WO 2002-JP835 | 20020201 |
| W: AR, AQ, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DT, EC, EE, ES, FI, GB, GD, GR, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, ME, MK, MN, MM, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW | | | | |
| RN: GH, GM, KE, LS, NM, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LJ, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| JP 2003137870 | A2 | 20030514 | JP 2001-331480 | 20011029 |
| CA 2437312 | AA | 20020815 | CA 2002-2437312 | 20020201 |
| JP 2002300897 | A2 | 20021015 | JP 2002-25423 | 20020201 |
| EP 1365029 | A1 | 20031126 | EP 2002-710461 | 20020201 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| CN 1633502 | A | 20050629 | CN 2002-807852 | 20020201 |
| US 2004030139 | A1 | 20040212 | US 2003-629865 | 20030730 |
| US 6965031 | B2 | 20051115 | | |
| PRIORITY APPLN. INFO.: | | | JP 2001-26316 | A 20010202 |
| | | | JP 2001-331480 | A 20011029 |
| | | | WO 2002-JP835 | W 20020201 |

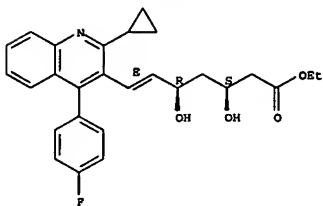
OTHER SOURCE(S): CASREACT 137:139496; MARPAT 137:139496
 GI

L9 ANSWER 15 OF 26 CA COPYRIGHT 2006 ACS on STN (Continued)



AB A process for producing the title compound (I) and optically active
 derivs.
 With microorganism by fermentation was given. I is useful as serum
 cholesterol-reducing agent. Preparation of Et ester of I (3R,5S-DOLE)
 and its
 derivs. 3S,5R-, 3S,5S-, and 3R,5R-DOLE with Saccharomycopsis fibuligera
 from 5-Mol, i.e.
 5-(E)-7-[2-cyclopropyl-4-(4-fluorophenyl)-quinolin-3-yl]-5-
 hydroxy-3-oxohept-6-enoic acid Et ester was shown.
 IT 147073-18-99
 RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP
 (Preparation)
 (process for producing
 (3R,5S)-(E)-7-[2-cyclopropyl-4-(4-fluorophenyl)-
 quinolin-3-yl]-3,5-dihydroxyhept-6-enoic acid ester and derive.)
 RN 167073-18-9 CA
 CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-
 dihydroxy-, ethyl ester, (3S,5R,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR
 THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE
 FORMAT

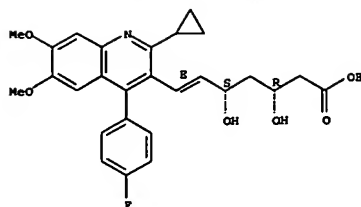
L9 ANSWER 15 OF 26 CA COPYRIGHT 2006 ACS on STN (Continued)

10/528179

L9 ANSWER 16 OF 26 CA COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 136:112193
 TITLE: Synthesis and biological evaluations of quinoline-based HMG-CoA reductase inhibitors
 AUTHOR(S): Suzuki, M.; Iwasaki, H.; Fujikawa, Y.; Kishihara, M.; Sakashita, M.; Sakoda, R.
 CORPORATE SOURCE: Central Research Laboratories, Nissan Chemical Industries, Ltd., Funabashi, Chiba, 274-8507, Japan
 SOURCE: Bioorganic & Medicinal Chemistry (2001), 9(10), 2727-2743
 CODEN: BMCEBP; ISSN: 0968-0896
 PUBLISHER: Elsevier Science Ltd.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 136:112193
 AB A series of quinoline-based 3,5-dihydroxyheptenoic acid deriva. were synthesized from quinolinecarboxylic acid esters by homologation, aldol condensation with Et acetoacetate dianion, and reduction of 3-hydroxyketone to evaluate their ability to inhibit the enzyme HMG-CoA reductase in vitro. In agreement with previous literature, a strict structural requirement exists on the external ring, and 4-fluorophenyl is the most active in this system. For the central ring, substitution on positions 6, 7, and 8 of the central quinoline nucleus moderately affected the potency, whereas the alkyl side chain on the 2-position had a more pronounced influence on activity. Among the deriva., NK-104 (pitavastatin calcium), which has a cyclopropyl group as the alkyl side chain, showed the greatest potency. We found that further modulation and improvement in potency at inhibiting HMG-CoA reductase was obtained by having the optimal substituents flanking the desmethylmevalonic acid portion, i.e., 4-fluorophenyl and cyclopropyl, instead of the usual iso-Pr group.
 IT 697234-82-5
 RL: RCT (Reactant); RACT (Reactant or reagent) (synthesis and biol. evaluations of quinoline-based HMG-CoA reductase inhibitors)
 RN 697234-82-5 CA
 CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-6,7-dimethoxy-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
 Double bond geometry as shown.

L9 ANSWER 16 OF 26 CA COPYRIGHT 2006 ACS on STN (Continued)



REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
 FORMAT

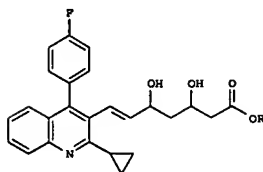
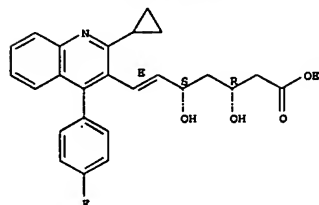
L9 ANSWER 17 OF 26 CA COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 136:36497 CA
 TITLE: Manufacture of (3R,5S,6E)-7-(substituted-quinolinyl)-3,5-dihydroxyhept-6-enoic acid esters by stereoselective enzymic hydrolysis
 INVENTOR(S): Tokuda, Shinichiro; Okabe, Tohiyuki; Soma, Tamotsu
 PATENT ASSIGNER(S): Nissan Chemical Industries, Ltd., Japan; Sanryo Kasei Kogyo K. K.
 SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.
 CODEN: JXXXXP
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|----------|
| JP 2001352996 | A2 | 20011225 | JP 2000-175316 | 20000612 |
| PRIORITY APPLN. INFO.: | | | JP 2000-175316 | 20000612 |

 OTHER SOURCE(S): MARPAT 136:36497
 GI

L9 ANSWER 17 OF 26 CA COPYRIGHT 2006 ACS on STN (Continued)

dihydroxy-, ethyl ester, (3R,5S,6E)- (9CI) (CA INDEX NAME)
 Absolute stereochemistry.
 Double bond geometry as shown.

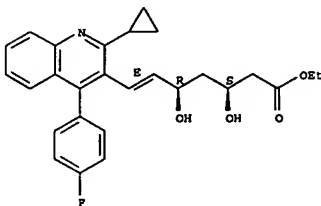


I

AB The compds. (3R,5S,6E)-I (R = C1-4 alkyl) (II), useful as intermediates for (3R,5S,6E)-7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxyhept-6-enoic acid salts as hypolipemics and antithrombotics, are manufactured by treating a mixture of stereoisomers of (6E)-I including II with acylating agents in the presence of hydrolases, removing the hydrolases from the reaction mixture, and then separating II from the mixture A mixture (3.37 g) of II (R = Et) 49.7, (3S,5R,6E)-I (R = Et) 49.7, (3S,5S,6E)-I (R = Et) <0.3, and (3R,5R,6E)-I (R = Et) <0.3% was treated with isopropenyl acetate and Lipase PS in Me3COMe at 40° for 94 h to give 1.40 g II (R = Et) with 99.4% e.e.
 IT 167073-19-0P
 RL: PUR (Purification or recovery); PREP (Preparation) (manufacture of optically-active quinolylidihydroxyheptenoic acid esters from stereoisomer mixts. using acylating agents and hydrolases)
 RN 167073-19-0 CA
 CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-

L9 ANSWER 18 OF 26 CA COPYRIGHT 2006 ACS on STN
 132:93197 CA
 TITLE: First systematic chiral syntheses of two pairs of enantiomers with 3,5-dihydroxyheptenoic acid chain, associated with a potent synthetic statin NK-104
 AUTHOR(S): Suzuki, Mikio; Yanagawa, Yoshinobu; Iwasaki, Hiroshi; Kanda, Hiroyasu; Yanagihara, Kazufumi; Matsumoto, Hiroo; Ohara, Yoshio; Yazaki, Yukari; Sakoda, Ryozo
 CORPORATE SOURCE: Central Research Institute, Nissan Chemical Industries
 SOURCE: Ltd., Chiba, 274-8507, Japan
 Bioorganic & Medicinal Chemistry Letters (1999), 9(20), 2977-2982
 CODEN: BMCL88; ISSN: 0960-894X
 PUBLISHER: Elsevier Science Ltd.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 132:93197
 AB All 4 enantiomers of the synthetic statin NK-104 were prepared. The syn diol isomers (NK-104 and its enantiomer) were obtained efficiently by diastereomer resolution. The anti diol isomers (3-epimer and 5-epimer) were prepared effectively by asym. aldol reaction followed by anti stereoselective reduction as key steps. Their purity detns. were effected by chiral HPLC anal.
 IT 147008-20-6P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of the enantiomers of NK-104)
 RN 147008-20-6 CA
 CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
 Double bond geometry as shown.

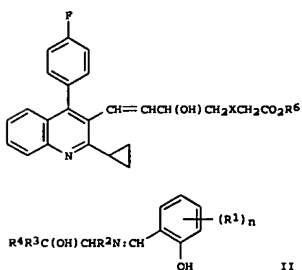


REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS

L9 ANSWER 19 OF 26 CA COPYRIGHT 2006 ACS on STN
 125:58345 CA
 TITLE: Preparation of optically active quinolyldihydroxyheptenoates as intermediates for anticholesteremics
 INVENTOR(S): Harada, Katsumasa; Matsushita, Akio; Sasaki, Hiroshi; Kawachi, Yasuhiro
 PATENT ASSIGNEE(S): Ube Industries, Ltd., Japan; Ube Kosan KK; Nissan Chemical Industries Ltd.
 SOURCE: Jpn. Kokai Tokkyo Koho, 9 pp.
 CODEN: JIXXAP
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-------------|------|----------|-----------------|----------|
| JP 08092217 | A2 | 19960409 | JP 1994-212958 | 19940906 |
| JP 3554036 | B2 | 20040811 | | |

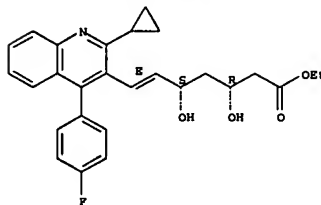
 PRIORITY APPLN. INFO.: JP 1994-212958 19940906
 OTHER SOURCE(S): CASREACT 125:58345; MARPAT 125:58345
 GI



AB The title compds. I (R6 = alkyl, Ph; X = CHOH) are prepared by reaction of (E)-3-[2-cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl]prop-2-en-1-ol (III) with diketene in organic solvents in the presence of Ti complexes, prepared from optically active Schiff bases II (R1 = alkyl; R2 = H, alkyl, Ph; R3, R4 = H, alkyl; R2 = R3 = R4 = H; n = 0-4) and Ti(OR5)4 (R5 = alkyl, Ph), followed by syn-reduction of the optically active I (X = CO). III and diketene were added to a mixture of (S)-II (R1 = 3-CMe3, R2 = CHMe2,

L9 ANSWER 18 OF 26 CA COPYRIGHT 2006 ACS on STN (Continued)
 RECORD. ALL CITATIONS AVAILABLE IN THE RECORD

L9 ANSWER 19 OF 26 CA COPYRIGHT 2006 ACS on STN (Continued)
 H) and Ti(OEt)4 in CH2Cl2 and stirred at -50° for 62 h to give 72% (5S)-(E)-I (R6 = Et, X = CO) with 78% ee, redn. of which with NaBH4 and Me2BOMe in THF-MeOH at -75° for 3.5 h gave 88% (3R,5S)-(E)-I (R6 = Et, X = CHOH) (IV). IV was converted into (4R,6S)-(E)-6-[2-cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl]ethenyl-4-hydroxy-3,4,5,6-tetrahydro-2H-pyran-2-one in 89% yield and 78% ee.
 IT 167073-19-0P
 RL: IMP (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of optically active quinolyldihydroxyheptenoates from quinolypropenal and diketene by addition with Ti complexes and reduction)
 RN 167073-19-0 CA
 CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)
 Absolute stereochemistry.
 Double bond geometry as shown.

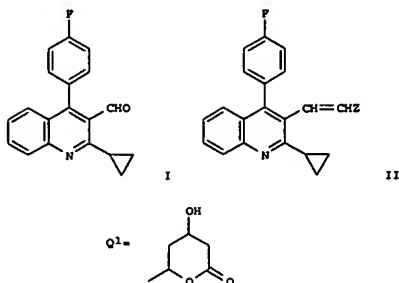


L9 ANSWER 20 OF 26 CA COPYRIGHT 2006 ACS on STN
 124:343135 CA
 TITLE: Preparation of quinoline type mevalonolactones
 Matsumoto, Hiroo; Kanda, Hiroyasu; Obara, Yoshio;
 Ikeda, Hirokazu; Murakami, Tatsufumi
 Daicel Kagaku Kogyo KK, Japan; Nissan Kagaku Kogyo KK
 Jpn. Kokai Tokkyo Koho, 10 pp.
 CODEN: JKKKAP
 Patent
 Japanese
 DOCUMENT TYPE:
 LANGUAGE:
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-------------|------|----------|-----------------|----------|
| JP 08003138 | A2 | 19960109 | JP 1995-35587 | 19950223 |
| JP 3739432 | B2 | 20060125 | | |

PRIORITY APPL. INFO.: JP 1994-28596 A 19940225

OTHER SOURCE(S): MARPAT 124:343135
 GI



AB The title compound I is prepared by reaction of olefin II [Z = Q1, etc.] with ozone. Thus, a mixture of ozone and oxygen was introduced into II [Z = Q1] in ethanol and methanol at -60 to -72° during 1.5 h. Dimethylsulfide was then added to the reaction mixture at -72°; and the resulting mixture was warmed to room temperature during 1 h to give, after

L9 ANSWER 21 OF 26 CA COPYRIGHT 2006 ACS on STN
 124:86587 CA
 TITLE: Process for producing optically active aromatic mevalonolactone compounds
 Ikeda, Hirokazu; Murakami, Tatsushi; Matsumoto, Hiroo;
 Obara, Yoshio; Kanda, Hiroyasu
 Daicel Chemical Industries, Ltd., Japan; Nissan Chemical Industries, Ltd.
 PCT Int. Appl., 31 pp.
 CODEN: PIXXD2
 Patent
 Japanese
 DOCUMENT TYPE:
 LANGUAGE:
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------|
| WO 9523125 | A1 | 19950831 | WO 1995-JP251 | 19950222 |
| W: AU, CA, CN, CZ, FI, HU, JP, KR, MX, NO, NZ, RO, RU, SI, US | | | | |
| RM: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| CA 2183071 | AA | 19950831 | CA 1995-2183071 | 19950222 |
| CA 2183071 | C | 20011218 | | |
| AU 9518231 | A1 | 19950911 | AU 1995-18231 | 19950222 |
| AU 691582 | B2 | 19980521 | | |
| EP 747341 | A1 | 19961211 | EP 1995-909953 | 19950222 |
| EP 747341 | B1 | 20020522 | | |
| R: AT, CH, DE, FR, GB, IT, LI, NL | | | | |
| HU 74486 | A2 | 19970128 | HU 1996-2291 | 19950222 |
| HU 214160 | B | 19980128 | | |
| AT 217859 | E | 20020615 | AT 1995-909953 | 19950222 |
| CN 1136182 | B | 20040128 | CN 1995-191678 | 19950222 |
| US 5929552 | A | 19990817 | US 1996-700396 | 19960822 |
| | | | JP 1994-28594 | 19940225 |

PRIORITY APPL. INFO.: WO 1995-JP251 W 19950222

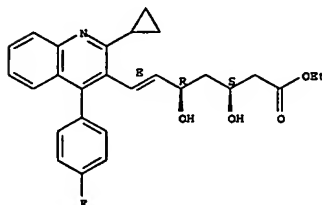
AB A mevalonolactone compound is produced by batchwise chromatog. or pseudo-moving bed method both using a column filled with a packing material for optical resolution comprising a polysaccharide derivative

The pseudo-moving bed method comprises jointing endlessly a number of columns to form a circulating flow path wherein a fluid is forcibly circulated in one direction, providing alternately along the direction of flow of the circulated fluid inlets for feeding the fluid into the column and outlets for drawing the fluid out of the column, moving intermittently the positions of the inlets and the outlets in the direction of flow of the circulated fluid, feeding a solution containing a racemate of a mevalonolactone compound and an eluent into a circulating path through the inlets, and drawing out simultaneously a solution enriched with nonadsorbates and a solution enriched with adsorbates through the outlets.

IT 172336-33-3
 RL: ANT (Analyte); ANST (Analytical study)
 (process for producing optically active mevalonolactone compound)
 RN 172336-33-3 CA
 CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolyl]-3,5-

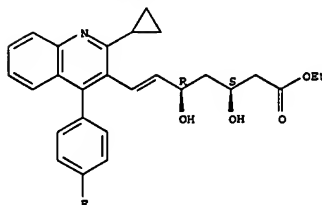
L9 ANSWER 20 OF 26 CA COPYRIGHT 2006 ACS on STN (Continued)
 workup, 29% I.
 IT 167073-18-99
 RL: PUR (Purification or recovery); PREP (Preparation)
 (preparation of quinoline type mevalonolactones)
 RN 167073-18-9 CA
 CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolyl]-3,5-dihydroxy-, ethyl ester, (3S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



L9 ANSWER 21 OF 26 CA COPYRIGHT 2006 ACS on STN (Continued)
 dihydroxy-, ethyl ester, [R-(R*,S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
 Double bond geometry unknown.



L9 ANSWER 22 OF 26 CA COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 123:168993 CA
 TITLE: Optically active β -aminoalkoxyborane complex as asymmetric reducing agent
 INVENTOR(S): Kashiwara, Hiroshi; Suzuki, Mikio; Ohara, Yoshio
 PATENT ASSIGNEE(S): Nissan Chemical Industries Ltd., Japan
 SOURCE: PCT Int. Appl., 91 pp.
 CODEN: PIXX02
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|------------------|-------------|
| WO 9417079 | A1 | 19940804 | WO 1994-JP56 | 19940117 |
| W: AU, CA, CN, CZ, FI, HU, KR, NO, NZ, RO, RU, UA, US | | | | |
| RM: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| JP 06329679 | A3 | 19941129 | JP 1993-332498 | 19931227 |
| TW 383309 | B | 20000301 | TW 1994-83100279 | 19940114 |
| CA 2153695 | AA | 19940804 | CA 1994-2153695 | 19940117 |
| AU 9458431 | A1 | 19940815 | AU 1994-58431 | 19940117 |
| AU 678427 | B2 | 19970529 | | |
| EP 680484 | A1 | 19951108 | EP 1994-904332 | 19940117 |
| EP 680484 | B1 | 19980819 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| CN 1116850 | A | 19960214 | CN 1994-190966 | 19940117 |
| CN 1047173 | B | 19991208 | | |
| HU 72018 | A2 | 19960328 | HU 1995-2184 | 19940117 |
| HU 217182 | B | 19991228 | | |
| AT 169921 | E | 19980915 | AT 1994-904332 | 19940117 |
| RU 2126412 | C1 | 19990220 | RU 1995-115845 | 19940117 |
| ZA 9400383 | A | 19940907 | ZA 1994-383 | 19940119 |
| IL 108387 | A1 | 20000629 | IL 1994-108387 | 19940120 |
| NO 9502870 | A | 19950919 | NO 1995-2870 | 19950719 |
| NO 305602 | B1 | 19990628 | | |
| US 5663348 | A | 19970902 | US 1995-481505 | 19950719 |
| US 5767277 | A | 19980616 | US 1997-779621 | 19970107 |
| US 5739347 | A | 19980414 | US 1997-848173 | 19970429 |
| US 5786405 | A | 19980728 | US 1997-848172 | 19970429 |
| US 5808098 | A | 19980915 | US 1997-848169 | 19970429 |
| US 5852221 | A | 19981222 | US 1997-848174 | 19970429 |
| NO 9805016 | A | 19950919 | NO 1998-5016 | 19981028 |
| CN 1234392 | A | 19991110 | CN 1999-105088 | 19990409 |
| PRIORITY APPL. INFO.: | | | JP 1993-7827 | A 19930120 |
| | | | JP 1993-66825 | A 19930325 |
| | | | WO 1994-JP56 | W 19940117 |
| | | | US 1995-481505 | A3 19950719 |

OTHER SOURCE(S): CASREACT 123:168993; MARPAT 123:168993
 GI

L9 ANSWER 22 OF 26 CA COPYRIGHT 2006 ACS on STN (Continued)

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

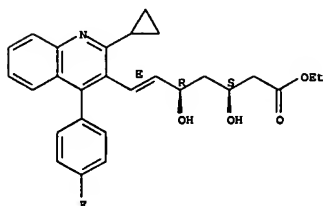
AB Optically active β -aminoalkoxyborane complexes are disclosed, specifically 1 (R1 = C1-C8 alkyl, C3-C7 cycloalkyl, C7-C11 aralkyl or C6-C10 aryl; R2 = H, C1-C8 alkyl, C3-C7 cycloalkyl or C7-C11 aralkyl; or R1R2 = (CH2)_n wherein n = 3 or 4; Ar = naphthyl, anthryl or phenanthryl, which may be substituted by 1-3 substituents selected from halo, nitro, C1-C6 alkyl, C3-C7 cycloalkyl, C2-C6 alkenyl or alkynyl, C7-C11 aralkyl, C6-C10 aryl, C1-C6 alkoxy, and styrene polymer substituent). The complexes are useful for reducing carbonyl compds. to optically active alcs., and especially for reducing 1,3-dicarbonyl compds. to optically active 1,3-syn-diols. For example, reduction of proline Et ester with LiAlH4 to give (S)-prolinol, cyclocondensation of this with β -naphthaldehyde to give an oxazolidine derivative (quant.), reduction of this with NaBH4 to give an amino alc. (quant.), and reaction of the latter with BH3.THF (quant.), gave the (S)-isomeric complex II. Reduction of diketo ester III using II and Et2BOMe in THF at 20° gave the (3S,5R)-syn-diol IV in 51% yield and 100% enantiomeric excess (ee). In contrast, several similar known borane complexes gave 28-78% yield but only 6-23% ee.

IT 167073-18-SP, (3S,5R)-Ethyl 7-[2-cyclopropyl-4-(p-fluorophenyl)quinolin-3-yl]-3,5-dihydroxy-6-heptenoate
 RL: IMP (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
 (reduction product; preparation of optically active β -aminoalkoxyborane complexes for asym. reduction of (di)carbonyl compds.)

RN 167073-18-9 CA
 CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3S,5R,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.

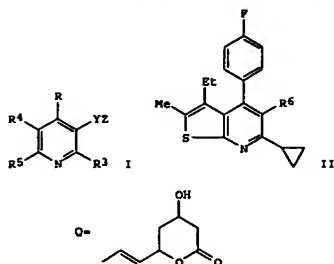
L9 ANSWER 22 OF 26 CA COPYRIGHT 2006 ACS on STN (Continued)



L9 ANSWER 23 OF 26 CA COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 119:117112 CA
 TITLE: Preparation of (heterocyclylvinyl)mevalonic lactone analogs as antiatherosclerotics
 INVENTOR(S): Saito, Yasushi; Kitahara, Masaki; Sakashita, Mitsueki
 PATENT ASSIGNEE(S): Toyota, Kyomi; Shibasaki, Toshie
 Nissan Chemical Industries, Ltd., Japan; Kowa Co., Ltd.
 SOURCE: Eur. Pat. Appl., 64 pp.
 CODEN: EPXKXW
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| EP 535548 | A1 | 19930407 | EP 1992-116417 | 19920924 |
| EP 535548 | B1 | 20011121 | | |
| R: AT, BE, CH, DE, DK, FR, GB, IE, IT, LU, NL, SE | | | | |
| JP 06329540 | A2 | 19941129 | JP 1991-257870 | 19911004 |
| JP 3130342 | B2 | 20010131 | | |
| AT 209035 | E | 20011215 | AT 1992-116417 | 19920924 |
| AU 9226012 | A1 | 19930408 | AU 1992-26012 | 19920928 |
| AU 652669 | B2 | 19940901 | | |
| NZ 244555 | A | 20000623 | NZ 1992-244555 | 19920930 |
| US 6162798 | A | 20001219 | US 1992-953716 | 19920930 |
| NO 9203858 | A | 19930405 | NO 1992-3858 | 19921002 |
| NO 302452 | B1 | 19980309 | | |
| CA 2079706 | AA | 19930415 | CA 1992-2079706 | 19921002 |
| CA 2079706 | C | 20040330 | | |
| HU 62794 | A2 | 19930628 | HU 1992-3138 | 19921002 |
| HU 214624 | B | 19980428 | | |
| CZ 281785 | B6 | 19970115 | CZ 1992-3027 | 19921002 |
| RU 2114620 | C1 | 19980710 | RU 1992-5052949 | 19921002 |
| SK 279277 | B6 | 19980909 | SK 1992-3027 | 19921002 |
| PRIORITY APPL. INFO.: | | | JP 1991-257870 | A 19911004 |

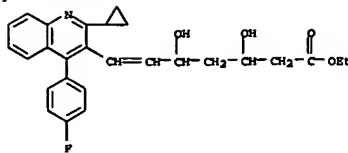
OTHER SOURCE(S): MARPAT 119:117112
 GI



AB Title compds. [I; R = substituted-Ph; R3 = H, (cyclo)alkyl, (cyclo)alkenyl, (substituted)Ph, etc.; R4R5 = atoms to complete a fused benzene or 5- or 6-membered heteroaryl ring; Y = CH2, CH2CH2, CH=CH, etc.; Z = 4-hydroxy-2-oxo- or 2,4-dioxo-6-tetrahydropyranyl, OCH2MCH2CO2R12, etc.; Q = CO, CH(OH), etc.; R12 = H, ammonium, physiol. labile ester residue, etc.; W = CO, CH(OH), etc.], inhibitors of atherosclerotic intimal thickening, were prepared. Thus, thienopyridinecarboxaldehyde II (R6 = CHO) was condensed with Bu4SnC(OEt):CH2 and the product hydrolyzed to give I [R6 = (E)-CH=CHCHO] which was condensed with MeCOCH2CO2Et to give, in 3 addnl. steps, II (R6 = oxopyranylvinyl group Q). The latter gave 100% inhibition of smooth muscle cell proliferation at 10⁻⁶ M (intimal) and 10⁻⁵ M (medial) in vitro.

IT 121661-13-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in preparation of antiatherosclerotic)

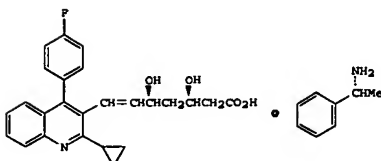
RN 121661-13-0 CA
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester (9CI) (CA INDEX NAME)



ACCESSION NUMBER: 118:233897 CA
TITLE: Preparation of diastereomer salt of optically active quinolinemevalonic acid
INVENTOR(S): Ohara, Yoshio; Suzuki, Mikio; Yanagawa, Yoshinobu; Iwasaki, Hiroshi; Miyachi, Nobuhide
PATENT ASSIGNEE(S): Nissan Chemical Industries, Ltd., Japan
SOURCE: Eur. Pat. Appl., 15 pp.
CODEN: EPXXDM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|-------------|
| EP 520406 | A1 | 19921230 | EP 1992-110636 | 19920624 |
| EP 520406 | B1 | 19980902 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, PT, SE | | | | |
| JP 05148237 | A2 | 19930615 | JP 1992-127277 | 19920520 |
| JP 3528186 | B2 | 20040517 | | |
| CA 2072162 | AA | 19921225 | CA 1992-2072162 | 19920623 |
| CA 2072162 | C | 20021119 | | |
| US 5284953 | A | 19940208 | US 1992-902863 | 19920623 |
| EP 742209 | A2 | 19961113 | EP 1996-107815 | 19920624 |
| EP 742209 | A3 | 19970514 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, PT, SE | | | | |
| AT 170513 | E | 19980915 | AT 1992-110636 | 19920624 |
| ES 2120973 | T3 | 19981116 | ES 1992-110636 | 19920624 |
| KR 208867 | B1 | 19990715 | KR 1992-11018 | 19920624 |
| US 5473075 | A | 19951205 | US 1992-123117 | 19930920 |
| US 5514804 | A | 19960507 | US 1995-450383 | 19950525 |
| PRIORITY APPLN. INFO.: | | | JP 1991-151810 | A 19910624 |
| | | | JP 1992-127277 | A 19920520 |
| | | | US 1992-902863 | A3 19920623 |
| | | | EP 1992-110636 | A3 19920624 |
| | | | US 1993-123117 | A3 19930920 |

GI



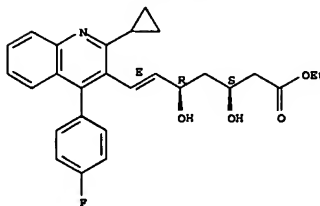
I

AB A diastereomer salt of the title compound (I) which is an intermediate for preparation of optically active quinolinemevalonic acid derive. with known biol. activity is prepared by resolution of its racemic parent. Et (2)-(E)-3,5-dihydroxy-7-[4-(4-fluorophenyl)-2-cyclopropyl-3-quinolinyl]-6-heptenoate in EtOH was added to 1N NaOH to give the free acid. To the CH2Cl2 solution of the free acid 1 equiv of D-(+)-PhCH(NH2)Me was added to give the (E)-(3R,5S)-I.

IT 147008-20-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(saponification of)

RN 147008-20-6 CA
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)

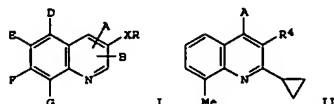
Relative stereochemistry.
Double bond geometry as shown.



L9 ANSWER 25 OF 26 CA COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 114:82195 CA
 TITLE: Preparation of 5-[3-(quinolinyl)vinyl- or ethyl]mevalonates as HMG-CoA reductase inhibitors
 INVENTOR(S): Philipps, Thomas; Angerbauer, Rolf; Fey, Peter; Huebsch, Walter; Bischoff, Hilmar; Petzinna, Dieter; Schmidt, Delf
 PATENT ASSIGNEE(S): Bayer A.-G., Germany
 SOURCE: Ger. Offen., 28 pp.
 CODES: GWXXBX
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-----------------------|------|-----------------|-----------------|----------|
| DE 3905908 | A1 | 19900906 | DE 1989-3905908 | 19890225 |
| PRIORITY APPL. INFO.: | | DE 1989-3905908 | | |

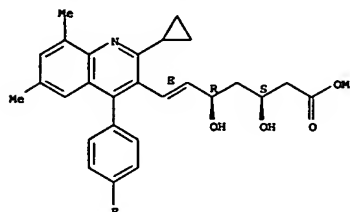
 OTHER SOURCE(S): CASREACT 114:82195; MARPAT 114:82195
 GI



AB The title compds. [I: A = (un)substituted heterocyclyl, aryl, alkyl; B = cycloalkyl, (un)substituted alkyl, aryl; D = H, alkyl; E, F, G = H, halo, alkyl; R = CH(OH)CH2CH2(OH)CH2CO2R2 or δ -lactone form thereof; R1 = H, alkyl; R2 = H, alkyl, aryl, cation; X = CH2CH2, CH=CH] were prepared. Thus, 2-amino-4'-fluoro-3-methylbenzophenone (preparation given) was cyclocondensed with R3COCH2CO2Me (R3 = cyclopropyl) to give quinolinecarboxylate II (A = 4-FC6H4) (III; R4 = CO2Me) which was converted in 2 steps to III (R4 = CHO). The latter was condensed with (EtO)2P(O)CH2CH2NR5 (R5 = cyclohexyl) and the product [III; (E)-CH:CHCHO] condensed with MeCOCH2CO2Me to give, after reduction, III (R4 = (E)-CH:CHCH(OH)CH2CH(OH)CH2CO2Me) which was 53 times as potent as mevinolin in inhibition of 3-hydroxy-3-methylglutaryl-CoA (HMG-CoA) reductase in vitro.
 IT 131775-33-2
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)
 (HMG-CoA reductase inhibitor activity of)
 RN 131775-33-2 CA
 CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-6,8-dimethyl-3-

L9 ANSWER 25 OF 26 CA COPYRIGHT 2006 ACS on STN (Continued)
 quinolinyl-1,3,5-dihydroxy-, methyl ester, (R*,S*-(E))- (9CI) (CA INDEX NAME)

Relative stereochemistry.
 Double bond geometry as shown.

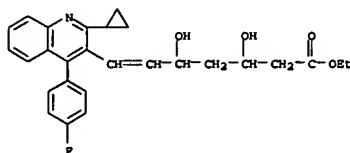


L9 ANSWER 26 OF 26 CA COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 111:134010 CA
 TITLE: Quinolinylheptenoic acid derivatives as anticholesteremics, their preparation, and formulations containing them
 INVENTOR(S): Fujikawa, Yoshihiro; Suzuki, Mikio; Iwasaki, Hiroshi; Sakashita, Mitsuaki; Kitahara, Masaki
 PATENT ASSIGNEE(S): Nissan Chemical Industries, Ltd., Japan
 SOURCE: Eur. Pat. Appl., 46 pp.
 CODES: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------------------------|-----------------|----------|
| EP 304063 | A2 | 19890222 | EP 1988-113448 | 19880818 |
| EP 304063 | A3 | 19901003 | | |
| EP 304063 | B1 | 19941130 | | |
| R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE | | | | |
| JP 01279866 | A2 | 19891110 | JP 1988-193606 | 19880803 |
| JP 2569746 | B2 | 19970108 | | |
| CA 1336714 | A1 | 19950815 | CA 1988-574999 | 19880817 |
| ES 2067460 | T3 | 19950401 | ES 1988-113448 | 19880818 |
| US 5011930 | A | 19910430 | US 1990-483720 | 19900223 |
| US 5102888 | A | 19920407 | US 1990-483724 | 19900223 |
| US 5185328 | A | 19930209 | US 1990-483829 | 19900223 |
| US 5872130 | A | 19990216 | US 1990-631092 | 19901219 |
| US 5856336 | A | 19990105 | US 1992-883398 | 19920515 |
| US 5854259 | A | 19981229 | US 1992-978884 | 19921119 |
| PRIORITY APPL. INFO.: | | JP 1987-207224 A 19870820 | | |
| | | JP 1988-15585 A 19880126 | | |
| | | JP 1988-193606 A 19880803 | | |
| | | US 1988-233752 A3 19880819 | | |
| | | US 1990-631092 A3 19901219 | | |
| | | US 1992-883398 A3 19920515 | | |

OTHER SOURCE(S): MARPAT 111:134010
 GI For diagram(s), see printed CA issue.
 AB The title compds. I [R1-R4, R6 = H, C1-6 alkyl, C3-6 cycloalkyl, C1-3 alkoxy, etc.; or R1 and R2, R3 and R4 may form CH:CHCH:CH, etc.; Y = CH2, CH2CH2, CH:CH, CH2CH:CH, CH:CHCH2; Z = OCH2MCH2CO2R12, Q1, etc.; Q = C(O), CH(OH), etc.; W = C(O), C(R11)(OH), etc.; R11 = H, C1-6 alkyl; R12 = H, R14; R14 = physiol. hydrolyzable alkyl, M; M = NH4, Na, K, etc.; R5 = H, C1-6 alkyl, C3-3 alkenyl, C3-6 cycloalkyl, etc.], useful as cholesterol biosynthesis inhibitors, were prepared. Reduction of Et (E)-7-[4'-(4'-fluorophenyl)-2'-(1'''-methylthyl)quinolin-3'-yl]-5-hydroxy-3-oxohept-6-enoate (preparation given) with NaBH4, followed by saponification in 0.5N NaOH, gave
 (E)-3,5-dihydroxy-7-[4'-(4'-fluorophenyl)-2'-(1'''-methylthyl)-quinolin-3'-yl]-hept-6-enoic acid Na salt (II). II exhibited an IC50 of 1.0 \pm 10-8M against cholesterol biosynthesis from acetate in vitro. A

L9 ANSWER 26 OF 26 CA COPYRIGHT 2006 ACS on STN (Continued)
 capsule formulation contg. II 1, lactose 3.5, cellulose 10, Mg stearate 0.5 g is given.
 IT 121661-13-0P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of, as cholesterol biosynthesis inhibitor)
 RN 121661-13-0 CA
 CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester (9CI) (CA INDEX NAME)



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(FILE 'HOME' ENTERED AT 14:33:52 ON 08 MAR 2006)

FILE 'REGISTRY' ENTERED AT 14:34:02 ON 08 MAR 2006

L1 STRUCTURE UPLOADED

L2 2 S L1 SAM

L3 24 S L1 FULL

FILE 'CA' ENTERED AT 14:34:31 ON 08 MAR 2006

L4 32 S L3

L5 83200 S LIQUID CHROMATOGRAPH?

L6 4 S L4 AND L5

L7 3 S L4 AND RESOLV?

L8 6 S L6 OR L7

L9 26 S L4 NOT L8

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---Logging off of STN---

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Executing the logoff script...

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STN INTERNATIONAL LOGOFF AT 14:35:46 ON 08 MAR 2006